REMARKS

Claim Amendments

Claims 1-2, 7-8 and 39-43 are pending herein. Claim 3 has been cancelled and Claim 1 has been amended to incorporate the subject matter of Claim 3. Support for all the amendments can be found throughout the specification and in the claims as originally filed. No new matter has been added.

Claim Objections

Claim 3 is objected to for not further limiting the claim on which it depends. Claim 3 has been cancelled herein and Claim 1 has been amended to incorporate the subject matter of Claim 3. Reconsideration and withdrawal of the objection are respectfully requested.

Claims 1-3, 7-8 and 40-43 are directed to statutory subject matter

Claims 1-3, 7-8 and 39-43 are rejected under 35 U.S.C. §101 because, according to the Office Action, the claimed invention is directed to non-statutory subject matter.

The claims have been amended as suggested by the Examiner. Reconsideration and withdrawal of the rejection is respectfully requested.

Rejection of Claims 1-3, 7-8 and 39-43 Under 35 U.S.C. §112, Second Paragraph

Claims 1-3, 7-8 and 39-43 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Office Action states that the claims have been rendered indefinite because of the recitation of the term "non-natural pyrimidine nucleoside".

Applicants respectfully disagree. The term "non-natural" is defined in the specification, as published, for example at paragraph [0060]. For the purposes of the invention, Applicants defined a base to be non-natural if it is not selected from the group consisting of thymine, guanine, cytosine, adenine and uracil. Moreover, the definition of C*pG and CpG* in the same paragraph demonstrates that terms "non-natural" and "analog" can be used interchangeably. Therefore, Claims 1-3, 7-8 and 39-43 meet the requirements of 35 U.S.C. §112. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-3, 7-8 and 42 are novel over Schwartz.

Claims 1-3, 7-8 and 42 are rejected under 35 U.S.C. §102(a) as being anticipated by Schwartz. Specifically, the Office Action states that Schwartz teaches modifying the dinucleotide CG with a modified C that can be cytosine arabinoside as evidenced by lines 5-15 of page 13 and Claim 4 of Schwartz.

Applicants respectfully disagree and do not feel that this is a correct reading of Schwartz. First, Schwartz specifically defines a modified ISS on page 10 as follows

> A composition of the subject invention is a modified ISS which is capable of eliciting a desired immune response upon administration. The term "modified ISS" as used herein refers to oligonucleotide sequences that effect a measurable immune response and comprise a CG dinucleotide in which the C residue is modified by addition to C-5 and/or C-6 of an electron-withdrawing moiety. Examples of measurable immune responses

Thus, even if the modified ISS of Schwartz can include arabinose as a sugar analog for the C within the CG dinucleotide, it would not make this C aracytosine because Schwartz requires that the C of the CG dinucleotide is modified to include an electron-withdrawing group at position C5 and/C6. Therefore, aracytosine cannot be a "modified C residue of a CG dinucleotide" according to Schwartz.

Accordingly, claims 1-3, 7-8 and 42 are novel over Schwartz. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-3, 7-8 and 41-42 are novel over Nguyen et al.

Claims 1-3 and 41-42 have been rejected under 35 U.S.C. §102(b) as being anticipated by Nguyen et al. According to the Office Action, Nguyen et al. teaches several oligonucleotide compounds comprising a dinucleotide of formula 5'-pyrimidine-purine-3', wherein the pyrimidine is linked to the purine via a phosphodiester.

Claims 1-3 and 41-42 have been amended to recite that the C* and G of the C*pG dinucleotide are linked via a phosphorothioate or phosphorodithioate linkage. As such, Nguyen et al. does not anticipate the instant claims. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-3 and 43 are novel over Clivio et al.

Claims 1-3 and 43 have been rejected under 35 U.S.C. §102(b) as being anticipated by Clivio et al. According to the Office Action, Clivio et al. teaches an oligonucleotide compound comprising a dinucleotide of formula 5'-pyrimidine-purine-3'.

Applicants respectfully disagree. It is well known to one skilled in the art that the immunostimulatory CpG dinucleotide comprises an unmethylated cytosine and occurs in the 5'->3' direction. The 14-mer of Clivio et al. does not recite a 5'-CpG-3' dinucleotide. As such, Clivio et al. does not anticipate the instant claims. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-3 and 40 are novel over Tardy-Planechaud et al.

Claims 1-3 and 40 have been rejected under 35 U.S.C. §102(b) as being anticipated by Tardy-Planechaud et al. According to the Office Action, Tardy-Planechaud et al. teaches an oligonucleotide compound comprising a dinucleotide of formula 5'-pyrimidine-purine-3', wherein the pyrimidine is linked to the purine via a phosphodiester.

Claims 1-3 and 40 have been amended to recite that the C* and G of the C*pG dinucleotide are linked via a phosphorothioate or phosphorodithioate linkage. As such, Tardy-Planechaud et al. does not anticipate the instant claims. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-3, 7 and 41 are novel over Butkus et al.

In response to the rejection over Butkus et al. in the previous Office Action (mailed from the USPTO on October 19, 2005, Claims 1, 2 and 41 were amended to change N4-alkylcytosine to N4-ethylcytosine. However, Claims 1, 2 and 42 have been amended back to N4-alkylcytosine.

The dinucleotide of Butkus et al. is linked via a phosphodiester linkage. Claims 1-3 and 40 have been amended to recite that the C* and G of the C*pG dinucleotide are linked via a phosphorothioate or phosphorodithioate linkage. As such, Butkus et al. does not anticipate the instant claims. Reconsideration and withdrawal of the rejection are respectfully requested.

Claim 39 is patentable over Kreutzer et al. in view of Schwartz

Claim 39 is rejected under 35 U.S.C. §103(a) as being unpatentable over Kreutzer et al. in view of Schwartz.

As stated above, Schwartz teaches a modified ISS comprising a CG dinucleotide in which the C residue is modified by addition to C-5 and/or C-6 of an electron withdrawing (hydrogen bond acceptor) group. The 5'-hydroxycytosine of Kruetzer has an added electron donating group (hydrogen bond donor).

Kreutzer describes the most common base substitutions arising from oxidative damage of DNA. Kreutzer does not describe immunostimulatory oligonucleotides or teaches the immunostimulatory properties of the oligonucleotides disclosed therein it cannot be considered art that is analogous to the Applicants endeavors.

As Schwartz specifically defines the modification to the CG dinucleotide and, as Schwartz states at page 7, lines 18 to 19, that when the same cytosine is methylated all immunostimulatory activity of the oligonucleotide is lost, one skilled in the art would not have been motivated, with a reasonable expectation of success, to combine the teachings of Schwartz with Kreutzer. Based on the teachings of Schwartz and Kreutzer, it would have been, at best, obvious-to-try modifiying the CG dinucleotide with 5'-hydroxycytosine.

The mere fact that the references could be combined to arrive at the claimed invention is not sufficient. The prior art must suggest the desirability of the combination. As Kruetzer deals with non-analogous art, and there is no mention in either Schwartz or Kreutzer of the desirability of combining their teachings, Claim 39 is patentable over Kreutzer et al. in view of Schwartz. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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